REMARKS

Applicants acknowledge the entry of the applicant's amendment filed on July 2, 2007. Claims 1, 32, 51, 88, 93, and 115 are hereby amended. Claims 3, 19-20, 34, 37, 41-42, 44, 46-47, 62-63, 80-81, 86-87, 89-90, 97, 99, and 110-111 are hereby canceled. No new matter has been added. Claims 1, 11, 14-18, 21-32, 38-39, 43, 45, 51-61, 64-70, 76-77, 82-85, 88, 93, 95-96, 103-104, 107-109, and 112-121 are now under consideration.

Applicants acknowledge that the information disclosure statements filed February 23, 2004 and July 2, 2007 have been reviewed to the extent the publication date was provided. Further to the Examiners request a complete list of co-pending and related applications is provided herein alongside an updated Information Disclosure Statement.

Applicants acknowledge that the arguments presented in the amendment filed on July 2, 2007 have been found persuasive by the Examiner and that the rejections and/or objections not reiterated from the previous Office Actions are withdrawn.

Claim 111 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Claim 111 is hereby canceled without prejudice to pursue the subject matter of the claim in a continuing application.

Claim 121 is objected to under 37 CFR 1.75 (c) as being in improper form. Claim 121 is hereby amended and made compliant with 37 CFR 1.75 (c).

Rejections under 35 U.S.C. § 112

Claims 1, 11, 14-32, 38, 39, 42, 43, 51, 56-70, 76, 77, 113 and 115 are rejected under 35 USC section 112, first paragraph, as failing to comply with the written description requirement. Applicants disagree with the Examiner's rejection. In the interest of advancing prosecution,

however, Applicants have amended claims 1 and 51 to specify that the patients treated are those with a symptom of constipation-predominant irritable bowel syndrome. Such patients may have constipation predominant IBS. It is also to be understood that such patients may have alternating constipation and diarrhea IBS, but at the time of treatment are experiencing a constipation predominant related symptom. Support for the amended claims can be found throughout the specification, for example in (paragraph [0019] page 2-3 of published application).

The Examiner alleges that the applicants disclosure is entirely silent with respect to the administration of methylnaltrexone in a treatment modality for IBS. Applicants respectfully request reconsideration. As described in the instant specification, "one of the underlying pathophysiological causes contributing to altered gut motility in IBS may be an interruption of normal peristalsis... (g)iven that endogenous opioids are possible mediators of gut segmentation and peristalsis...applicants believe that a peripherally acting opioid such as methylnaltrexone would be beneficial in the treatment of IBS' (paragraph [0019] page 2-3 of published application). Example 1 of the instant invention shows that the administration of methylnaltrexone in 12 normal subjects (8 male and 4 female) who were not receiving opioids significantly reduced oral-cecal transit time. Increased oral-cecal transit time is one of the symptoms of IBS (Hutchinson R. et al, Gut, 1995; 35: 585-589). Applicants submit that this is evidence that methylnaltrexone would be useful to treat a subject with symptoms of constipation-predominant IBS (paragraph [0147] page 14-15 of published application).

The Examiner alleges that there is no description of an administration regimen directed to distinct subsets of patient populations or to the various symptoms of IBS and of multiple drug therapy. In addition to the example discussed in more detail above, the specification describes methods for treating IBS by the administration of methylnaltrexone to distinct subsets of patient populations (paragraph [0033] of the published specification). The various symptoms of IBS that may be ameliorated by the methods of the instant invention are discussed in detail in paragraph [0023]. The multiple drugs that can be used with methylnaltrexone to treat IBS according to the methods of the invention are discussed in paragraphs [0024, 0049-0090]. The modes of

administration, formulations including their manufacture, effective amounts and dosages of methylnaltrexone to be used in the treatment of IBS according to the methods of invention are described in paragraphs [0025-0032, 0037-0039, 0091-0144] and Examples 2-5 of the published application. Applicants respectfully direct the examiners attention to the above referenced paragraphs of the instant specification. The referenced paragraphs in addition to the data from Example 1 discussed above provide sufficient description of the instant invention to reasonably convey to the skilled artisan that the Applicants at the time of the filing of the invention had possession of the claimed invention.

The Examiner states that treatment regimens are prophetic and that no working examples are provided that would describe to one of ordinary skill in the art an embodiment that meets all of the limitations of claims. Applicants respectfully disagree. Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether a (working) example is disclosed. An applicant need not have actually reduced the invention to practice prior to filing. *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987). The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Because only an enabling disclosure is required, applicant need not describe all actual embodiments. As discussed above in greater detail, Example 1 shows that methylnaltrexone can affect peristalsis in patients that are not receiving opioids. In combination with the results from Example 1, the instant specification provides sufficient guidance for one of ordinary skill in the art to practice the invention. Therefore, Applicants respectfully request withdrawal of the rejection.

Double patenting

Claims 88, 93, 95, 96, 103, 104, 107-114 and 116-121 are provisionally rejected on the ground of non-statutory obviousness type double patenting as being unpatentable over claims 13-29, 32, 33 and 39-44 Co-Pending Application Number 11/441452. Applicant understands that in accordance with section 804 of the MPEP, a "provisional" double patenting rejection will continue

to be made by the Examiner until the "provisional" double patenting rejection is the only rejection remaining in one of the applications. Accordingly, Applicant will address the appropriateness of these "provisional" double patenting rejections after the Examiner withdraws all other reasons for rejection.

Rejection under 35 U.S.C. § 102

Claims 1, 11, 14, 16-18, 27, 29, 31, 43, 45, 51-55, 57-59, 82-85, 103, 104, 107, 108, 111 and 116 are rejected under 35 U.S.C. 102(a) as being anticipated by Levine, J.D. US 2004/0180916 (herein after Levine). Applicants respectfully request reconsideration. The statutory language of 35 U.S.C. 102(a) "known or used by others in this country" means knowledge or use which is accessible to the public. A patent application is not evidence of such public knowledge or use as of its filing date. For 35 U.S.C. 102(a) to apply to the Levine published application, Levine must have a publication date earlier in time than the effective filing date of the instant application. The earliest publication date of Levine is September 16, 2004 (July 01, 2004 for the related PCT WO04054511). The filing date of the instant application is April 8, 2004. Therefore rejection of the instant claims under 35 U.S.C. 102(a) over Levine is not appropriate. Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 103(a)

Claims 1, 11, 14-27, 29-32, 38, 39. 42, 44-45, 51-68,70, 76, 77, 82-85, 88, 93, 95, 96, 103, 104, 107, 108, and 110-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levine, J.D. US 2004/0180916 (herein after Levine) in view of The Merck Manual, and De Schryver et al., Scand. J. Gastroenterology. Applicants respectfully request reconsideration.

As discussed above, Levine does not qualify as prior art under § 102 (a). Levine also does not qualify as prior art under paragraph (e) of 35 U.S.C. § 102for the purpose of the present rejection. Levine published under Section 122 (b) and the filing date of Levine is December 12, 2003, prior to the filing date of the instant application. Applicants also point out that the Levine priority document, U.S. Provisional Application No. 60/433,217 filed on December 13, 2002, does

not disclose the administration of methylnaltrexone to treat pain associated with IBS. Hence, the Examiner can rely only on Levine's filing date of December 12, 2003 for the disclosure of methylnaltrexone to treat IBS.

However, the present application is identical to its priority document, U.S. Provisional Application No. 60/461,608, filed April 8, 2003, which fully supports the instant claims. Applicants, therefore, can rely on the priority date of April 8, 2003 which precedes the Levine filing date. Levine, therefore, is not prior art to the present application as of its filing date.

The effective filing date of the instant application predates the disclosure of methylnaltrexone by Levine. Accordingly, Levine is not prior art under Section 35 U.S.C. § 102 and can not be used as basis for a rejection under Section 35 U.S.C. § 103 (a) of the instant claims. Applicants respectfully request withdrawal of the rejection.

CONCLUSION

Claims 1, 11, 14-18, 21-32, 38-39, 43, 45, 51-61, 64-70, 76-77, 82-85, 88, 93, 95-96, 103-104, 107-109 and 112-121 are under examination. In view of the foregoing amendments and remarks, it is requested that the rejections under 35 U.S.C. sections 112, 102 and 103 be withdrawn If the Examiner believes, after this amendment, that a telephone call with the undersigned would advance prosecution of this application, the Examiner is requested to call the undersigned at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: March 14, 2008

Respectfully submitted,

By _____
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